

REMARKS

In the Office Action mailed March 16, 2006,

Claims 11, 48, 49, 50 and 58 were indicated to be allowable.

Claim 57, 64 and 65 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, and were further rejected under 35 U.S.C. 103(a) as unpatentable over Frazier et al. in view of Pisano et al. and Lin et al and Say et al.

Claims 1-8, 10, 12, 25-27, 31, 34, 36-37, 50, 60, 67, 68 and 70 were rejected under 35 U.S.C. 103(a) as being unpatentable over Frazier et al.(WO 01/93930) in view of Pisano et al. (US 5,928,207). It is respectfully submitted that claim 50 has been included in this rejection by typographical error because claim 50 has been indicated to be allowable.

Claims 9, 13-15, 18,19 and 20-24 were rejected under 35 U.S.C. 103(a) as unpatentable over Frazier et al. in view of Pisano et al., as applied to claims 1-8, 10, 12, 25-27, 31, 34, 36-37 and 60 above, further in view of Say et al.(US 6,134,461).

Claims 1-10, 12-15, 18,19, 20-27, 31, 34, 36-37, 50, 60, and 67-70 were rejected under 35 U.S.C. 103(a) as being unpatentable over Frazier et al.(WO 01/93930) in view of Pisano et al. (US 5,928,207). It is respectfully submitted that claim 50 has been included in this rejection by typographical error because claim 50 has been indicated to be allowable.

Claims 16 and 17 were rejected under 35 U.S.C. 103(a) as unpatentable over Frazier et al. in view of Pisano et al. and Say et al, as applied to claims 9,13-15, 18, 19 and 21-24 above, further in view of Meade et al. (US 5,770,369)

Claim 20 was rejected under 35 U.S.C. 103(a) as unpatentable over Frazier et al. in view of Pisano et al. and Say et al., as applied to claims 9,13-15, 18, 19 and 21-24, further in view of Lin et al.

CLAIM AMENDMENTS AND ADDITIONS

Claim 1 has been amended to recite that applicants' biosensor microprobe device does not have a closed fluid channel in any portion of the device that passes into the subject during penetration to access the fluid. Applicants submit that no new matter has been entered with this amendment.

Claim 57 has been amended to depend from claim 1, and claim 64 amended to depend from claim 57. Claims 57, 64 and 65 have been amended so that the entire area of the

microprobe including the tip and excluding the body end has a uniform thickness that is less than the thickness of the body. The applicants submit that the term "uniform thickness" allows for some acceptable degree of unintended variation from perfect uniformity, e.g., due to limitations of the process used to fabricate the microprobe portion. As such, the applicants submit that no new matter has been entered with this amendment.

NEW CLAIMS

New claim 71 has been added to recite that the microprobe device has a biosensor which comes into direct contact with the bodily fluid and is located sufficiently close to the penetration end, that it penetrates at least part way through the skin. Applicants submit that no new matter has been added with this new claim.

CLAIM REJECTIONS

Claims 68-70

Claims 68-70 have been cancelled without prejudice. The applicants submit that the rejections of claims 68-70 are moot in view of the cancellation of these claims.

Claims 1-10, 12-27, 31, 34, 36-37 and 60

Claim 1 was rejected under 35 U.S.C. 103(a) as unpatentable over Frazier et al.(WO 01/93930) in view of Pisano et al. (US 5,928,207). Claim 1 has been amended to recite that applicants' biosensor microprobe device does not have a closed fluid channel in any portion of the device that passes into the subject during penetration to access the fluid. In operation, the hollow microneedle of Frazier et al. is inserted through the skin, causing the distal end of the closed fluid channel to penetrate into the subject. A biosensor is deposited on at least one wall of the closed channel and analyte-containing bodily fluid drawn over the sensor. For fluid withdrawal or delivery, the closed channel must penetrate into the subject to permit transport of the fluid through the channel.

Claim 1 was also rejected under 35 U.S.C. 103(a) as unpatentable over Frazier et al.(WO 01/93930) in view of Pisano et al. (US 5,928,207), and further in view of Say et al. (US 6,134,461).

Frazier et al. teach the virtues of their closed channel hollow microneedle device for fluid injection and extraction. The device can also monitor analyte concentrations of both injected and extracted fluids. Applicants submit that removal of the closed channel would destroy device use for fluid injection, or for fluid extraction using the variety of pumping and transducer mechanisms taught (page 6, lines 29-32, page 7 lines 1-13). Similarly, monitoring of analyte concentrations in these fluids would not be possible. There is therefore no motivation in Frazier et al. to remove the closed channel from their device.

Frazier et al. further teach the advantages of a bioluminescence-based biosensor, which provides substantial sensitivity and accuracy over a wide concentration range (Frazier et al. page 18, lines 12-15). Frazier et al. teach that this type of biosensor, which emits light rather than producing an electric signal, can be deposited on one or more inner walls of the closed channel of a hollow microneedle (Frazier et al. page 18) in order to sense analyte presence in fluid drawn into the channel. Frazier et al. also teach the use of the closed channel itself to transfer the

emitted light to an optical detector. Generally, detection of the emitted light is performed at the output ports of the microneedle (Frazier et al. page 18, lines 11-12). The optical detector may be inside microneedle or may detect the light through a window in the wall (Frazier et al. page 19, lines 21-25). Furthermore, Frazier et al. teach the use of a light enhancing reflective coating on the inside surfaces of the closed channel to enhance the light output generated during a bioluminescent reaction, providing greater detection sensitivity (page 15, lines 30-34).

Say discloses a structure where the sensor is located at the penetration end of the device, and is connected to the body portion via wires. There is no closed channel in Say's device. Applying the configuration of Say to Frazier, the bioluminescent-based biosensor would be located on the probe substrate at the penetration end. During use, the probe would penetrate into the subject and access the analyte-containing bodily fluid. Without a closed channel, essentially all the light emitted by the biosensor would be lost into the body of the subject and not reach the optical detector even if the latter (e.g. a photodiode) were also located on the penetration end of the substrate, close to the biosensor.

Since Frazier teaches the virtues of a closed fluid channel as both a waveguide a means of enhancing light emission one of skill in the art would not be motivated to remove the closed channel as taught by Say. Furthermore, removing the closed fluid channel would destroy the function of the device taught by Frazier since there would be no way for the light to reach the sensor. Thus there would be no technological motivation for combining Frazier with Say. As such these two references are not properly combinable and a prima facie case of obviousness cannot properly be made regarding the applicant's invention. See *in re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Therefore, the applicant submits that claim 1, as it now stands, fully satisfies the requirements of 35 U.S.C. § 103 and is patentable thereunder.

Say et al. further teach that the probe substrate is a non-conductive (therefore high resistivity) material. Nowhere do Say et al. disclose or suggest that the substrate should be single-crystal silicon as claimed by applicants. Single-crystal silicon is a semiconductor, a poorer insulator than the substrates taught by Say. Say et al. teach that the sensor is formed directly on the surface of a "variety of non-conducting materials, including, for example, polymeric or plastic materials and ceramic materials." Col. 7, lines 52-54. The ceramic materials include aluminum oxide and silicon dioxide. Col. 8, lines 14-15. Applicants submit that use of single crystal silicon in the device of Say as taught by Pisano would destroy the function of the

invention of Say, which requires a non-conducting substrate. As such there would be no motivation to combine Say with Pisano and a prima facie case of obviousness is not present (see *in re Gordon*).

Furthermore, claims 2, 5-10, 12, 26-27, 31, 34 and 37 depend from claim 1 and recite additional features therefor, claims 3-4 depend from claim 2, claims 13, 25 depend from claim 12, claims 14, 16, 18 depend from claim 13, claim 15 depends from claim 14, claim 17 depends from claim 16, claims 19-24 depend from claim 18, claim 36 depends from claim 34, and claim 60 depends from claim 5. As such, and for the same reasons set forth above, the applicants submit that these dependent claims define an invention suitable for patent protection.

Claims 57, 64, and 65

Claims 57, 64, and 65 were rejected under 35 U.S.C. 112, first paragraph. These claims have been amended to require a uniform thickness over the entire area of the microprobe portion, including the point, that is thinner than the thickness of the body portion. Applicants submit that these claims now contain no new matter. Claims 57, 64, and 65 were further rejected under 35 U.S.C. 103(a) as unpatentable over Frazier et al. in view of Pisano et al. and Lin et al. and Say et al. As the Office Action states, the Frazier/Pisano combination does not teach the relative thicknesses of the needle and body.

Lin et al. teach a device with a uniform 50 micrometer thickness over the entire body (shank end 12, FIG. 2B) (column 7, lines 40-4) and along an adjacent section of the microprobe portion (shaft 14, FIG. 2A) (column 4, lines 22-24). The tip end of the shaft is then etched, tapering irregularly on the sides and bottom to form a small, sharp terminal point. Claims 57, 64, and 65, as currently amended, teach that the entire microprobe portion of applicants' device, including any terminal point, (equivalent to the entire shaft including tip region in Lin et al.) has a uniform thickness that is less than the thickness of the body (shank). This thinning of the microprobe portion minimizes pain upon penetration into the arm. Lin et al.'s microneedle, by contrast, is designed to penetrate brain tissue, which does not experience pain. Lin et al. teach that a thicker shaft provides strength (column 9, lines 36-38 and 57-59), thus teaching the benefit of maintaining the shank thickness in the shaft portion, but also teach that a small terminal point is required to fit between adjacent neural cells (column 10, line 1). Further, the etching technology of Lin et al. cannot produce a shaft that has a uniform thickness across the shaft or

along the tip. Accordingly, Lin et al. do not teach or suggest all the limitations of claims 57, 64, or 65 as amended.

Say et al. teach a device of uniform thickness with a point formed in the X-Y plane. Nowhere do Say et al. teach or suggest a microprobe device with a uniform thickness over the entire area of the microprobe portion, including the point, that is thinner than the thickness of the body portion. Applicants submit that a prima facie case of obviousness has not been established because even in combination Frazier et al, Pisano et al., Lin et al. and Say et al. fail to disclose all the features recited in claim 57, 64 and 65 as amended.

The applicants submit that the rejections of:
claims 9, 13-15, 18 and 20-24 over Frazier et al. in view of Pisano et al., as applied to
claims 1-8, 10, 12, 25-27, 31, 34, 36-37, 50 and 60 further in view of Say et al.,
claims 9 and 13-15 under 35 U.S.C. 103(a) over Frazier et al. in view of Say et al.,
claims 16 and 17 Frazier et al. in view of Pisano et al. and Say et al further in view of
Meade et al., and
the rejection of claim 20 over Frazier et al. in view of Pisano et al. and Say et al, as
applied to claims 9, 13-15, 18, 19 and 21-24, in further view of Lin et al.,
are overcome by virtue of their dependence on claims that are believed to be allowable for the
reasons discussed above.

Declaration under 37 C.F.R. §1.13135 regarding U.S.C. §103(a) Rejections

Claims 1-10, 12-27, 31, 34, 36-37, 57, 60, 64-65 and 67-70 were rejected by the Examiner under 35 U.S.C. 103(a) as being obvious over International Patent Publication WO 01/93930 A1 to Frazier et al ("Frazier") in view of other art. The arguments made in the response above are believed to have been fully satisfactory in overcoming these rejections. Nevertheless, in the interest of advancing prosecution, a Declaration has been submitted pursuant to 37 C.F.R. §1.131 by one of the inventors, Wilson Smart. The Declaration establishes that the subject matter of the present application was invented prior to the filing date of Frazier. Frazier was filed on June 1, 2001, less than ten months before the filing date of the present application. Frazier claims priority to U.S. provisional application 60/208,868, which was filed on June 2, 2000. The inventor states that Exhibits 1 and 2 were developed prior to June 2, 2000, the earliest possible priority date for the subject matter in Frazier. Additionally, one of the inventors, Wilson Smart, states that he diligently worked on this

technology and on developing the patent application from its conception until at least June 1, 2001. Hence, it is clear that the subject matter disclosed and claimed in the present application was invented before June 2, 2000. Therefore, the Applicants respectfully request that the 35 U.S.C. § 103(a) rejections based on Frazier be withdrawn.

Information Disclosure Statement

A supplemental information disclosure statement (IDS) has been included with his amendment to correct the date of a reference included in the previous IDS submitted December 21, 2005 and to add a new reference of which applicants had not been aware. It is respectfully submitted that initialed copies of both these IDS be returned with the next communication from the Patent Office

CONCLUSION

In view of the foregoing, applicants believe that all of the claims are now in condition for allowance. The applicants therefore respectfully request reconsideration of the application and a notice of allowance. If for any reason the Examiner believes any of the claims are not in condition for allowance, he is encouraged to phone Joshua D. Isenberg (Reg. No. 41,088) at (650) 849-7777 so that any remaining issues may be resolved.

Respectfully submitted,

Date: Sept 18, 2006

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